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A wearable haemodialysis device: one day at a time, the first step to continuous treatment

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## Abstract

A wearable haemodialysis device potentially holds out the promise to the dialysis patient freedom to carry on with their life, without dietary and fluid restrictions. A recent trial reported on treating patients for 24 hours, a small but important step forward in the development of a wearable device.

Words 1001

3 million patients with chronic kidney disease are treated world-wide by haemodialysis. Although this would suggest that haemodialysis is a successful life supporting treatment, one only has to scratch under the surface to realise that the 5 year survival in economically advanced is less than that for several common solid organ malignancies [1]. In addition haemodialysis is an expensive treatment which limits availability to patients in economically developing countries.

Haemodialysis requires a dialyzer with rapid small solute clearance through which blood and dialysate are pumped in counter-current directions. Sessions typically last 4 hours or less thrice weekly. Due to the intermittent treatment patients are requested to restrict dietary intake of sodium, potassium, phosphate, and fluid intake to limit weight gains between dialysis sessions. During the haemodialysis session fluid that has accumulated is removed, so the commonest complication during haemodialysis is hypotension. The rapid clearance of small solutes leads to changes in plasma osmolality and reverse water movement into the brain, so in addition to symptoms related to hypotension, most patients feel tired post dialysis, and this fatigue may take from minutes to more than a day to resolve [2]. Although some patients benefit from home haemodialysis, the majority dialyse in dialysis centres, often having to adapt their life style to fixed sessions and the time spent travelling to and from centres. Not surprisingly many patients are unable to continue with employment, and self-reported depression rates are high [3].

Gura and colleagues now report on the use of a wearable haemodialysis device [4]. A wearable device would potentially allow patients to mobilise during treatment, so allowing them to move around and perform normal activities. In addition by working 24 hours a day, it would allow slower removal of both fluid and uraemic toxins, so potentially reducing inter-dialytic symptoms and the risk of hypotension. To be acceptable to the patient the wearable the device has to be lightweight and ergonomically comfortable to wear. On the other hand the device has to operate for as long as possible, so that the patient does not have to regularly replace parts [5]. Compared to the standard haemodialysis treatment, the device uses a fixed dialysate

volume of 375 ml, which then has to be regenerated by passing through a series of sorbents and ion exchangers. As these do not substantially remove urea, urea is enzymatically converted by urease added to the sorbents to ammonia, which is then converted into ammonium carbonate, leading to the generation of carbon dioxide [6]. To prevent bubbles of carbon dioxide disrupting flow in the dialysate circuit, a gas permeable section of tubing was inserted between the sorbents and the dialyzer. A battery operated single mini-pump powered blood and dialysate in counter-current directions through a standard dialyzer. Four additional pumps were required to regulate ultrafiltration flow, administration of heparin for anticoagulation, and one each for an electrolyte mixture and sodium bicarbonate solution used to refresh the dialysate.

Seven patients were treated, connected to the wearable haemodialysis device using central venous access catheters. Five patients completed the 24 hour treatment. Ideally this device would be worn at home, and as such the first hurdle is to establish safety. One patient stopped using the device due to circuit clotting, another due to multiple technical problems. Two patients required battery exchanges for the blood pump. Three patients required interventions to remove air bubbles from the blood circuit, thought to have come from air left within the dialyzer during initial circuit priming. One patient had to have the sorbent cartridges replaced. A common problem encountered was small bubbles of carbon dioxide which were not fully eliminated by the gas permeable chamber, and these would intermittently reduce dialysate flows. As patients were allowed to move around freely, then blood flows intermittently fell due to mechanical kinking of blood lines. These later problems can be overcome by redesign of the circuit, increasing the capacity of the gas permeable section, and using different plastic polymers for the blood and dialysate lines.

In terms of clearances, as expected with the much slower blood ( $42\pm 24$  ml/min) and dialysate ( $43\pm 20$  ml/min) flows, the instantaneous clearances were much lower than during a standard conventional haemodialysis session. However whereas the clearance of urea with standard intermittent haemodialysis would be substantially greater than that for creatinine, and creatinine much greater than for phosphate, clearances with the wearable device were very similar; urea  $17\pm 10$  ml/min, creatinine  $16\pm 8$  ml/min and phosphate  $15\pm 9$  ml/min. Patients started treatment very shortly after completing a standard haemodialysis treatment, and blood urea concentrations did increase over the 24 hour treatment period, suggesting that the amount of urease in the sorbent cartridges was unable to cope with urea generation rates. Blood flows appeared to decline after 16 hours, so clearances did fall in most patients (Figure). However the rise in blood urea was apparent after 8 hours, before this reduction in blood flow. On the other hand although  $\beta_2$  microglobulin clearance was lower at  $5\pm 4$  ml/min, serum  $\beta_2$  microglobulin levels did not rise, suggesting that  $\beta_2$  microglobulin removal was equal to

the production rate [7]. This suggests a key advantage for the wearable device, as larger solutes, and in particular those protein bound uraemic toxins are not effectively cleared by conventional haemodialysis [8], whereas they would potentially be cleared by the wearable device.

Patients tolerated treatment very well. They were allowed to eat and drink, and 1002±380 ml was removed by ultrafiltration, with no significant change in blood pressure [9], although blood pressure appeared to be a little lower after 8 hours of treatment. More importantly patient feedback in terms of lack of inter-dialytic symptoms, zero to minimal recovery time post treatment was very positive. In addition patients were equally positive in their perception of the potential for this device in terms of allowing treatment flexibility, freedom and improved life style. Although a small step forward in the development of a wearable haemodialysis device, the device worked and the concept remains on course. Lessons were learnt for a redesigned version for future clinical trials.

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Figure. Average clearance of urea, creatinine, phosphate,  $\beta_2$  microglobulin and corresponding blood and dialysate flows.

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